(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 20 December 2001 (20.12.2001)

PCT

(10) International Publication Number WO 01/96353 A3

(51) International Patent Classification⁷: 19/16, A61K 31/7068, A61P 31/12

C07H 19/06,

1 15/00,

(21) International Application Number: PCT/US01/19147

(22) International Filing Date: 15 June 2001 (15.06.2001)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/212,100

15 June 2000 (15.06.2000) US

- (71) Applicants (for all designated States except US):
 NOVIRIO PHARMACEUTICALS LIMITED [—/—];
 Walker Secretaries, Walker House, Grand Cayman (KY).
 CENTRE NATIONAL DA LA RECHERCHE SCIENTIFIQUE (CNRS) [FR/FR]; 3, rue Michel-Ange, F-75794 Paris Cedex 16 (FR).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): BRYANT, Martin, L. [US/US]; 65 Hickory Lane, Carlisle, MA 01741 (US). GOSSELIN, Gilles [FR/FR]; 82, rue Calvin, 400, Avenue Paul Rimbaud, F-34080 Montpellier (FR). IMBACH, Jean-Louis [FR/FR]; 1108, rue las Sorbes, Impasse des Luques, F-34000 Montpellier (FR).
- (74) Agent: KNOWLES, Sherry, M.; King & Spalding, 191 Peachtree Street, Atlanta, GA 30303-1763 (US).

- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 18 April 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

3 A3

(54) Title: 3'-PRODRUGS OF 2'-DEOXY-β-L-NUCLEOSIDES

(57) Abstract: The present invention relates to compounds, compositions and methods for the treatment of a host infected with a hepatitis B virus. Specifically, compounds and compositions of 3'-esters of 2'-deoxy-β-L-nucleosides are disclosed, which can be administered either alone or in combination with other anti-hepatitis B agents. Compounds and compositions of 3',5'-esters of 2'-deoxy-β-L-nucleosides are disclosed, which can be administered either alone or in combination with other anti-hepatitis B agents, are also disclosed.

INTERNATIONAL SEARCH REPORT

Inter onal Application No PCT/US 01/19147

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 CO7H19/06 CO7H CO7H19/16 A61K31/7068 A61P31/12 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) CO7H A61K A61P Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category * WO 00 09531 A (NOVIRIO PHARMACEUTICALS 1 - 194X LIMITE; IMBACH JEAN LOUIS; GOSSELIN GILLES) 24 February 2000 (2000-02-24) cited in the application the whole document 1-4,6-8 V. SKARIC ET AL.: "Aminoacyl derivatives X of 4-thiothymidine, cytosine and cytidine" CROATICA CHEMICA ACTA, vol. 48, no. 3, 1976, pages 351-359, XP001034973 page 352 -/--Patent family members are listed in annex. Further documents are listed in the continuation of box C. Special categories of cited documents: *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the *A* document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-*O* document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means document published prior to the international filing date but later than the priority date claimed *&* document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 21/02/2002 28 November 2001 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040. Tx. 31 651 epo nl. de Nooy, A Fax: (+31-70) 340-3016

3

INTERNATIONAL SEARCH REPORT

Inter one Application No
PCT/US 01/19147

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WANG P ET AL: "RECENT ADVANCES IN L-NUCLEOSIDES: CHEMISTRY AND BIOLOGY" ANTIVIRAL RESEARCH, ELSEVIER SCIENCE BV., AMSTERDAM, NL, vol. 46, no. 1/2, 1998, pages 19-44, XP000944025 ISSN: 0166-3542 scheme 2 conclusions	1,156
X	US 5 559 101 A (WEIS ALEXANDER L ET AL) 24 September 1996 (1996-09-24) the whole document	1,2
X	WO 92 08727 A (CONSIGLIO NAZIONALE RICERCHE ;MENARINI RICERCHE SUD SPA (IT)) 29 May 1992 (1992-05-29) the whole document	1,2
X ·	BOUDOU V ET AL: "A new and convenient approach for the synthesis of ribo- and 2'-deoxyribo-beta-L-furanonucleosides starting from beta-L-xylofuranonucleosides" NUCLEOSIDES & NUCLEOTIDES, MARCEL DEKKER, INC, US, vol. 18, no. 45, 1999, pages 607-609, XP002164642 ISSN: 0732-8311 the whole document	1,156
A	RYU E K ET AL: "AMINOACYL DERIVATIVES OF NUCLEOSIDES, NUCLEOTIDES, AND POLYNUCLEOTIDES. XXVII GENERAL SYNTHESIS OF 2'(3')-O-AMINOACYL DINUCLEOSIDE PHOSPHATES DERIVED FROM THE AA-TRNA TERMINUS" JOURNAL OF CARBOHYDRATES. NUCLEOSIDES NUCLEOTIDES, MARCEL DEKKER, BASEL, CH, vol. 4, no. 6, 1977, pages 387-408, XP000564974 ISSN: 0094-0585 structures 4b-e	4

3

INTERNATIONAL SEARCH REPORT

information on patent family members

Inter. onal Application No PCT/US 01/19147

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 0009531	A	24-02-2000	AU CN EP WO	5475799 A 1320128 T 1104436 A2 0009531 A2	06-03-2000 31-10-2001 06-06-2001 24-02-2000
US 5559101	A	24-09-1996	EP JP WO	0788506 A2 10507772 T 9613512 A2	13-08-1997 28-07-1998 09-05-1996
WO 9208727	A	29-05-1992	IT AU WO	1246983 B 8923291 A 9208727 A1	12-12-1994 11-06-1992 29-05-1992